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TI rhoB encoding a UV-inducible Ras-related small GTP-binding protein is regulated by GTPases of the Rho family and independent of JNK, ERK, and p38 MAP kinase.

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AB The small GTPase RhoB is immediate-early inducible by DNA damaging treatments and thus part of the early response of eukaryotic cells to genotoxic stress. To investigate the regulation of this cellular response, we isolated the gene for rhoB from a mouse genomic library. Sequence analysis of the rhoB gene showed that its coding region does not contain introns. The promoter region of rhoB harbors regulatory elements such as TATA, CAAT, and Sp1 boxes but not consensus sequences for AP-1, Elk-1, or c-Jun/ATF-2. The rhoB promoter was activated by UV irradiation, but not by 12-O-tetradecanoylphorbol-13-acetate treatment. rhoB promoter deletion constructs revealed a fragment of 0.17 kilobases in size which was sufficient in eliciting the UV response. This minimal promoter fragment contains TATA and CAAT boxes but no other known regulatory elements. Neither MEK inhibitor PD98059 nor p38 kinase inhibitor **SB203580** blocked stimulation of rhoB by UVC (UV light, 254 nm) which indicates that ERK or p38 mitogen-activated protein (MAP) kinase are not involved in the UV induction of rhoB. Also, phosphatidylinositol 3-kinase inhibitor wortmannin, which blocks UV stimulation of both JNK and **p38** MAP kinase, did not **inhibit** rhoB activation. Furthermore, activation of JNK by interleukin-1beta did not affect rhoB expression. These data indicate that JNK is not involved in the regulation of rhoB. Overexpression of wild-type Rac as well as the Rho guanine-dissociation inhibitor caused activation of rhoB. Wild-type RhoB inhibited both basal and UV-stimulated rhoB promoter activity, indicating a negative regulatory feedback by RhoB itself. The data provide evidence both for a signal transduction pathway independent of JNK, ERK, and p38 MAP kinase to be involved in the induction of rhoB by genotoxic stress, and furthermore, indicate autoregulation of rhoB.

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